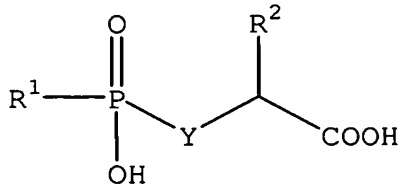
WE CLAIM:

1. A method for treating opioid tolerance comprising administering an effective amount of a NAALADase inhibitor to a mammal in need of such treatment.

2. The method of claim 1, wherein the NAALADase inhibitor is an acid containing a metal binding group.

3. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula I



I

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

Y is CR^3R^4, NR^5 or O;

R^1 is hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, Ar, $COOR^6$, NR^6R^7 or OR^6, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s) which are, for example, independently selected from carboxy, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, $COOR^6$, NR^6R^7 and Ar;

R^2 is hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, Ar, halo or carboxy, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s) which are, for example, independently selected from carboxy, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, NR^6R^7 and Ar;

R^3 and R^4 are independently hydrogen or C_1-C_3 alkyl;

R^5 is hydrogen or C_1-C_3 alkyl;

R^6 and R^7 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl or Ar, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s) which are, for example, independently selected from carboxy, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy and Ar; and

Ar is selected from 1-naphthyl, 2-naphthyl, 2-indolyl, 3-indolyl, 4-indolyl, 2-furyl, 3-furyl, tetrahydrofuranyl, tetrahydropyranyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-pyridyl, 4-pyridyl and phenyl, wherein said Ar is unsubstituted or substituted with one or more substituent(s) which are, for example, independently selected from halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, C_2-C_6 alkenyloxy, phenoxy, benzyloxy, carboxy and N^6R^7.

4. The method of claim 3, wherein Y is CH_2.

5. The method of claim 4, wherein R^2 is $-(CH_2)_2COOH$.

6. The method of claim 5, wherein R^1 is hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, benzyl, phenyl or OR^6, wherein said alkyl, alkenyl, cycloalkyl, cycloalkenyl, benzyl and phenyl are independently unsubstituted or substituted with one or more substituent(s) independently selected from carboxy, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, halo, hydroxy, nitro, trifluoromethyl, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_1-C_6 alkoxy, C_2-C_6 alkenyloxy, phenoxy, benzyloxy, NR^6R^7, benzyl and phenyl.

7. The method of claim 6, wherein the compound of formula I is selected from:

2-(phosphonomethyl)pentanedioic acid;

2-[[(2-carboxyethyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

2-[(benzylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[(phenylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[[((hydroxy)phenylmethyl)hydroxyphosphinyl]-methyl]pentanedioic acid;

2-[(butylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[[(3-methylbenzyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

2-[(3-phenylpropylhydroxyphosphinyl)methyl]-pentanedioic acid;

2-[[(4-fluorophenyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

2-[(methylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[(phenylethylhydroxyphosphinyl)methyl]pentanedioic acid;

2-[[(4-methylbenzyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

2-[[(4-fluorobenzyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

2-[[(4-methoxybenzyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

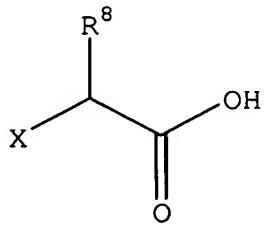
2-[[(3-trifluoromethylbenzyl)hydroxyphosphinyl]-methyl]pentanedioic acid;

2-[[4-trifluoromethylbenzyl)hydroxyphosphinyl]-methyl]pentanedioic acid;

2-[[(2-fluorobenzyl)hydroxyphosphinyl]methyl]-pentanedioic acid;

2-[[(2,3,4,5,6-pentafluorobenzyl)hydroxy-phosphinyl]methyl]pentanedioic acid; and enantiomers and pharmaceutically acceptable equivalents.

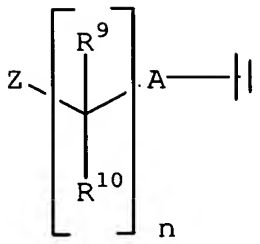
8. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula II



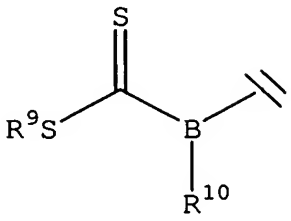
II

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

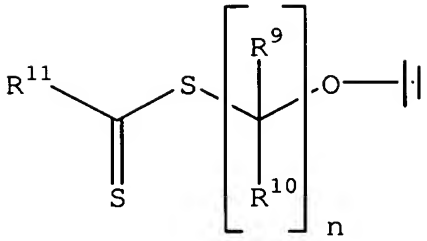
X is a moiety of formula III, IV or V



III



IV



V ;

Z is SH, SO_{3H}, SO_2H, SOH, $SO(NH)R^{12}$ or $S(NHR^{12})_2R^{13}$;

B is N or CR^{14};

A is O, S, $CR^{15}R^{16}$ or $(CR^{15}R^{16})_mS$;

m and n are independently 0, 1, 2, 3 or 4;

R^8, R^9, R^{10}, R^{11}, R^{12}, R^{14}, R^{15} and R^{16} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_3-C_8 cycloalkyl, C_5-C_7 cycloalkenyl, Ar^1, hydroxy, carboxy, carbonyl, amino, cyano, isocyano, nitro, sulfonyl, sulfoxy, thio, thiocarbonyl, thiocyano, formanilido, thioformamido, sulfhydryl, halo, haloalkyl, trifluoromethyl or oxy, wherein said alkyl, alkenyl, cycloalkyl and cycloalkenyl are independently unsubstituted or substituted with one or more substituent(s); and

Ar^1 is a carbocyclic or heterocyclic moiety, which is unsubstituted or substituted with one or more substituent(s);

provided that when X is a moiety of formula III and A is O, then n is 2, 3 or 4; when X is a moiety of formula III and A is S, then n is 2, 3 or 4; and when X is a moiety of formula III and A is $(CR^{15}R^{16})_mS$, then n is 0, 2, 3 or 4.

9. The method of claim 8, wherein:

X is a moiety of formula III;

n is 0, 1, 2 or 3;

Z is SH, SO_3H, SO_2H, SOH or $S(NHR^{12})_2R^{13}$; and

A is O, S or $CR^{15}R^{16}$.

10. The method of claim 9, wherein Z is SH.

11. The method of claim 10, wherein R^8 is $-(CH_2)_2COOH$.

12. The method of claim 10, wherein the compound of formula II is selected from:

2-(2-sulfanylethyl)pentanedioic acid;

3-(2-sulfanylethyl)-1,3,5-pentanetricarboxylic acid;

2-(2-sulfanylpropyl)pentanedioic acid;

2-(2-sulfanylbutyl)pentanedioic acid;

2-(2-sulfanyl-2-phenylethyl)pentanedioic acid;

2-(2-sulfanylhexyl)pentanedioic acid;

2-(2-sulfanyl-1-methylethyl)pentanedioic acid;

2-[1-(sulfanylmethyl)propyl]pentanedioic acid;

2-(3-sulfanylpentyl)pentanedioic acid;

2-(3-sulfanylpropyl)pentanedioic acid;

2-(3-sulfanyl-2-methylpropyl)pentanedioic acid;

2-(3-sulfanyl-2-phenylpropyl)pentanedioic acid;

2-(3-sulfanylbutyl)pentanedioic acid;

2-[3-sulfanyl-2-(phenylmethyl)propyl]pentanedioic acid;

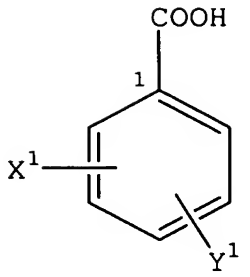
2-[2-(sulfanylmethyl)butyl]pentanedioic acid;

2-[2-(sulfanylmethyl)pentyl]pentanedioic acid;

2-(3-sulfanyl-4-methylpentyl)pentanedioic acid; and

enantiomers and pharmaceutically acceptable equivalents.

13. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula VI



VI

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^1 is -W-Z^1;

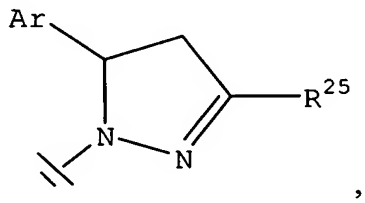
W is a bond or a linking group;

Z^1 is a terminal group; and

Y^1 is -COOH oriented *meta* or *para* relative to C-1.

14. The method of claim 13, wherein:

X^1 is -$(CR^{17}R^{18})_nNH(CR^{19}R^{20})_mCOOH$, -$PO(OH)OR^{22}$, -$(CR^{17}R^{18})_nP(O)(OH)R^{22}$, -NH-$(CR^{19}R^{20})_m$-heteroaryl, -$NH(P(O)(R^{23})OH)$, -$(CR^{17}R^{18})_nNH(P(O)(OH)R^{23})$, -$CON(R^{22})(OH)$ -$(CR^{17}CR^{18})_nCON(R^{22})(OH)$, -$(CR^{17}R^{18})_nSH$ or -$O(CR^{19}R^{20})_mSH$, -SO_2NH-aryl, -N(C=O)-CH_2(C=O)-aryl, -SO_2NH-aryl, -N(C=O)-CH_2(C=O)-aryl, -O-aryl wherein aryl in -O-aryl is substituted by at least one of nitro, carboxy or



,

wherein X^1 is oriented *meta* or *para* relative to C-1;

m and n are independently 1-3, provided that when X^1 is -$O(CR^{19}R^{20})_mSH$, then m is 2 or 3;

R^{17}, R^{18}, R^{19}, R^{20}, R^{22}, R^{23} and R^{25} are independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino or C_1-C_6 alkoxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl,

carbocycle, heterocycle and alkoxy are independently unsubstituted or substituted with one or more substituent(s); and

Y^1 is -COOH oriented *meta* or *para* relative to C-1.

15. The method of claim 13, wherein the compound of formula VI is selected from:

2-[(4-carboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

2-[(2,5-dicarboxyphenyl)sulfonyl]-1,4-benzene-dicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

2-[(2-carboxyphenyl)thio]-1,4-benzenedicarboxylic acid;

2-nitro-1,4-benzenedicarboxylic acid;

2-bromo-1,4-benzenedicarboxylic acid;

2-amino-1,4-benzenedicarboxylic acid;

2-sulfoterephthalic acid, monosodium salt;

2-carboxymethyl-1,4-benzenedicarboxylic acid;

2-[(2-furanylmethyl)-amino]-1,4-benzenedicarboxylic acid;

2-[(carboxymethyl)amino]-1,4-benzenedicarboxylic acid;

4-(4-nitrobenzoyl)-1,3-benzenedicarboxylic acid;

4-[4-(2,4-dicarboxybenzoyl)phenoxy]-1,2-benzene-dicarboxylic acid;

4-[[(2,4,6-trimethylphenyl)amino]carbonyl]-1,3-benzenedicarboxylic acid;

4-nitro-1,3-benzenedicarboxylic acid;

4-[(1-naphthalenylamino)-carbonyl]-1,3-benzene-dicarboxylic acid;

1,2,4-benzenetricarboxylic acid;

4-[(2-carboxyphenyl)thio]-1,3-benzenedicarboxylic acid;

4-[3-[[3-(2,4-dicarboxyphenoxy)propyl]dithio]-propoxy]-1,3-benzenedicarboxylic acid;

4-hydroxy-1,3-benzenedicarboxylic acid;

4-[(2-furanylmethyl)amino]-1,3-benzenedicarboxylic acid;

4-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid;

5-[4,5-dihydro-5-(4-hydroxyphenyl)-3-phenyl-1H-pyrazol-1-yl]-1,3-

benzenedicarboxylic acid;

5-(4,5-dihydro-3-methyl-5-phenyl-1H-pyrazol-1-yl)-1,3-benzenedicarboxylic acid;

5-[[(4-chloro-3-nitrophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-[[[4-chloro-3-[[3-(2-methoxyphenyl)-1,3-dioxopropyl]amino]phenyl]amino]sulfonyl-1,3-benzenedicarboxylic acid;

5-[[3-[4-(acetylamino)phenyl]-1,3-dioxopropyl]amino]-1,3-benzenedicarboxylic acid;

5-acetylamino-1,3-benzenedicarboxylic acid;

5-[[(1-hydroxy-2-naphthalenyl)carbonyl]-methylamino]-1,3-benzenedicarboxylic acid;

5-(4-carboxy-2-nitrophenoxy)-1,3-benzenedicarboxylic acid;

5-sulfo-1,3-benzenedicarboxylic acid;

5-nitro-1,3-benzenedicarboxylic acid;

5-amino-1,3-benzenedicarboxylic acid;

1,3,5-benzenetricarboxylic acid;

5-[[(3-amino-4-chlorophenyl)amino]sulfonyl]-1,3-benzenedicarboxylic acid;

5-(3-mercaptopropoxy)-1,3-benzenedicarboxylic acid;

5-hydroxy-1,3-benzenedicarboxylic acid;

5-(2-mercaptoethoxy)-1,3-benzenedicarboxylic acid;

5-[(hydroxyamino)carbonyl]-1,3-benzenedicarboxylic acid;

5-phosphono-1,3-benzenedicarboxylic acid;

5-mercaptomethyl-1,3-benzenedicarboxylic acid;

5-phosphonomethyl-1,3-benzenedicarboxylic acid;

5-[[(carboxymethyl)amino]-methyl]-1,3-benzene-dicarboxylic acid;

5-[(carboxymethyl)amino]-1,3-benzenedicarboxylic acid;

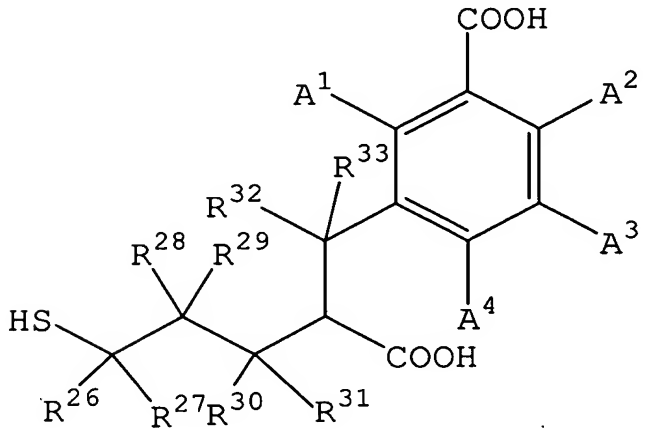
5-[[(2-furanylmethyl)amino]-methyl]-1,3-benzene-dicarboxylic acid;

5-[2-(hydroxyamino)-2-oxoethyl]-1,3-benzene-dicarboxylic acid;

5-(2-mercaptoethyl)-1,3-benzenedicarboxylic acid; and

enantiomers and pharmaceutically acceptable equivalents.

16. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula VII



VII

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32} and R^{33} are independently hydrogen or C_1-C_3 alkyl;

A^1, A^2, A^3 and A^4 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halo, nitro, phenyl, phenoxy, benzyl, benzyloxy or -COOH, or any adjacent two of A^2, A^3 and A^4 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic ring, said heterocyclic aromatic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s).

17. The method of claim 16, wherein:

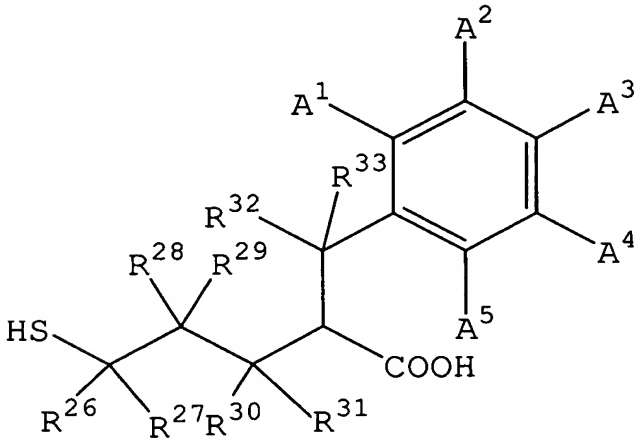
R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32} and R^{33} are independently hydrogen or methyl; and

A^1, A^2, A^3 and A^4 are independently hydrogen, C_1-C_4 alkyl, C_1-C_2 alkoxy, halo, nitro, phenyl, phenoxy, benzyloxy, nitro or -COOH.

18. The method of claim 16, wherein any adjacent two of A^2, A^3 and A^4 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic

ring, said heterocyclic aromatic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s).

19. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula VIII



VIII

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32} and R^{33} are independently hydrogen or C_1-C_3 alkyl; and

A^1, A^2, A^3, A^4 and A^5 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, C_1-C_3 perhaloalkyl, phenyl, phenoxy, benzyl, benzyloxy, hydroxy, halo, cyano, nitro, $-SO_2R^{34}$, $-(C=O)NR^{34}R^{35}$, $-(C=O)NR^{34}(CH_2)_nCOOH$, $-NR^{34}(C=O)R^{35}$, $-(CH_2)_nCOOH$ or –COOH, or any adjacent two of A^1, A^2, A^3, A^4 and A^5 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic ring, said heterocyclic aromatic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s);

R^{34} and R^{35} are independently hydrogen, C_1-C_6 alkyl, phenyl or benzyl; and

n is 1-3.

20. The method of claim 19, wherein:

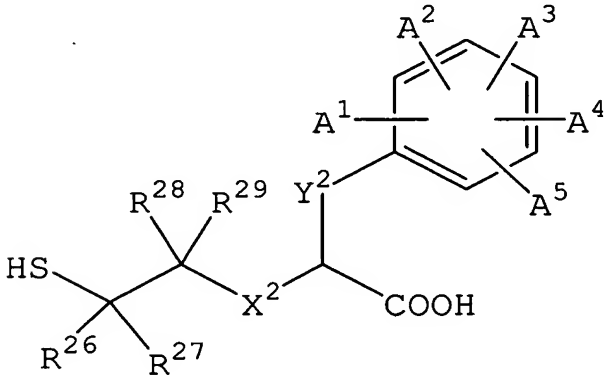
R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{32} and R^{33} are each hydrogen;

A^1, A^2, A^3, A^4 and A^5 are independently hydrogen, C_1-C_4 alkyl, C_1-C_2 alkoxy, C_1-C_2 perhaloalkyl, phenyl, phenoxy, hydroxy, halo, cyano, nitro, $-SO_2R^{34}$, $-(C=O)NR^{34}R^{35}$, $-(C=O)NR^{34}(CH_2)COOH$, $-NR^{34}(C=O)R^{35}$ or $-(CH_2)COOH$; and

R^{34} and R^{35} are independently hydrogen, methyl or benzyl.

21. The method of claim 19, wherein any adjacent two of A^1, A^2, A^3, A^4 and A^5 form with the benzene ring a fused 5- or 6-membered carbocyclic or heterocyclic aromatic ring, said heterocyclic aromatic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s).

22. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula IX



IX

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^2 and Y^2 are independently $-CR^{30}R^{31}$-, -O-, -S- or $-NR^{30}$-, provided that at least one of X^2 and Y^2 is/are $-CR^{30}R^{31}$-;

A^1, A^2, A^3, A^4 and A^5 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, $-COOR^{34}$, $-COR^{34}$, $-NR^{34}R^{35}$, $-SR^{34}$, $-SOR^{34}$, $-SO_2R^{34}$, $-SO_2(OR^{34})$, $-(C=O)NR^{34}R^{35}$, $-(C=O)NR^{34}(CH_2)_nCOOH$, $-NR^{34}(C=O)R^{35}$ or $-(CH_2)_nCOOH$, or any adjacent two of A^1, A^2, A^3, A^4 and A^5 form with the benzene ring a fused ring that is saturated or unsaturated, aromatic or non-aromatic, and carbocyclic or heterocyclic, said heterocyclic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s);

n is 1-3;

R^{26}, R^{27}, R^{28}, R^{29}, R^{30}, R^{31}, R^{34} and R^{35} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy,

benzyloxy, and fused ring are independently unsubstituted or substituted with one or more substituent(s).

23. The method of claim 22, wherein:

Y^2 is –O-, -S- or $–NR^{30}$-;

A^1, A^2, A^3, A^4 and A^5 are independently hydrogen, C_1-C_4 alkyl, C_1-C_2 alkoxy, hydroxy, halo, -COOH, $-COR^{34}$, $-NR^{34}(C=O)R^{35}$ or $-(CH_2)COOH$; and

R^{34} and R^{35} are independently hydrogen or methyl.

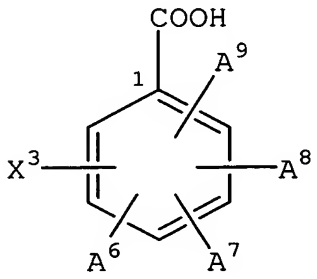
24. The method of claim 22, wherein:

Y^2 is $–CR^{30}R^{31}$-;

A^1, A^2, A^3 and A^4 are each hydrogen; and

A^5 is phenoxy, benzyloxy, aryl, heteroaryl, carbocycle or heterocycle, wherein said phenoxy and benzyloxy are substituted with –COOH, and said aryl, heteroaryl, carbocycle and heterocycle are independently substituted with one or more substituent(s) selected from cyano and –COOH.

25. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula X



X

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^3 is $-(CR^{36}R^{37})_nSH$, $-O(CR^{36}R^{37})_2SH$, $-S(CR^{36}R^{37})_2SH$ or $-NR(CR^{36}R^{37})_2SH$;

n is 1-3; and

R, R^{36}, R^{37}, A^6, A^7, A^8 and A^9 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkylsulfonyl, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle,

heterocycle, alkoxy, alkenoxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s).

26. The method of claim 25, wherein the compound of formula X is selected from:

3-(2-mercaptoethyl)-benzoic acid;

3-(mercaptomethyl)-benzoic acid;

2-(mercaptomethyl)-benzoic acid;

5-hydroxy-2-(2-mercaptoethyl)-benzoic acid;

2-(2-mercaptoethyl)-benzoic acid;

5-[(4-carboxyphenyl)methoxy]-2-(2-mercaptoethyl)-benzoic acid;

2-(2-mercaptoethyl)-5-(phenylmethoxy)-benzoic acid;

2-(carboxymethoxy)-6-(2-mercaptoethyl)-benzoic acid;

5-[(3-carboxyphenyl)methoxy]-2-(2-mercaptoethyl)-benzoic acid;

2-(2-mercaptoethyl)-6-(phenylmethoxy)-benzoic acid;

2-[(2-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(4-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

3-(2-mercaptoethyl)-[1,1'-biphenyl]-2,3'-dicarboxylic acid;

2-(3,3-dimethylbutoxy)-6-(2-mercaptoethyl)-benzoic acid;

2-(2-mercaptoethyl)-6-(2-phenylethoxy)-benzoic acid;

2-[(2-chlorophenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[[3-carboxy-5-(1,1-dimethylethyl)phenyl]methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-(2-mercaptoethyl)-6-phenoxy-benzoic acid;

2-(2-mercaptoethyl)-6-phenylamino-benzoic acid;

2-(2-mercaptoethyl)-6-(phenylthio)-benzoic acid;

5'-(1,1-dimethylethyl)-3-(2-mercaptoethyl)-[1,1'-biphenyl]-2,3'-dicarboxylic acid;

3-(2-mercaptoethyl)-[1,1'-biphenyl]-2,4'-dicarboxylic acid;

2-[(4-carboxy-2-methoxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(4-carboxy-3-methoxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(2-bromo-4-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(3-bromo-4-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(4-chlorophenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-(biphenyl-2-ylmethoxy)-6-(2-mercaptoethyl)-benzoic acid;

2-[(3-bromo-5-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(2-bromo-5-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-(2-mercaptoethyl)-6-[(4-methoxyphenyl)methoxy]-benzoic acid;

2-(2-mercaptoethyl)-6-[(4-methylphenyl)methoxy]-benzoic acid;

2-[(4-bromo-3-carboxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

2-[(2-carboxy-5-methoxyphenyl)methoxy]-6-(2-mercaptoethyl)-benzoic acid;

5-(mercaptomethyl)-2-(2-phenylethoxy)-benzoic acid;

2-bromo-5-(mercaptomethyl)-benzoic acid;

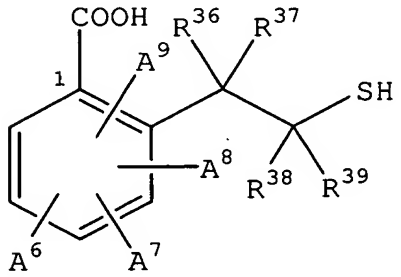
4-(mercaptomethyl)-[1,1'-biphenyl]-2,3'-dicarboxylic acid;

5-(mercaptomethyl)-2-(phenylmethoxy)-benzoic acid; and

4-bromo-3-(mercaptomethyl)-benzoic acid; and

enantiomers and pharmaceutically acceptable equivalents.

27. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XI



XI

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

R^{37}, R^{38}, R^{39} and R^{40} are independently hydrogen or C_1-C_3 alkyl;

A^6, A^7, A^8 and A^9 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkylsulfonyl, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenoxy,

phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s).

28. The method of claim 27, wherein:

R^{36}, R^{37}, R^{38} and R^{39}, A^7, A^8 and A^9 are each hydrogen;

A^6 is hydrogen, $-(CH_2)_n-W^1$, or $-Y^3-(CH_2)_n-W^1$;

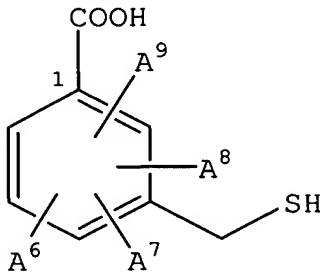
n is 0-3;

Y^3 is O, S or NR^{40};

R^{40} is hydrogen or C_1-C_4 alkyl; and

W^1 is C_1-C_6 alkyl or phenyl, wherein W^1 is unsubstituted or substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, carboxy or halo.

29. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XII



XII

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

A^6, A^7, A^8 and A^9 are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkylsulfonyl, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenoxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s).

30. The method of claim 29, wherein:

A^7, A^8 and A^9 are each hydrogen;

A^6 is $-(CH_2)_n-Ar^2$ or $-Y^3-(CH_2)_n-Ar^2$;

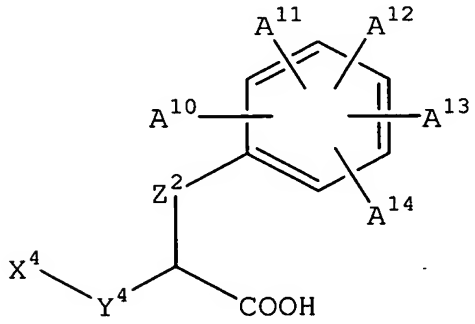
n is 0-3;

Y^3 is O, S or NR^{41};

R^{41} is hydrogen or C_1-C_4 alkyl; and

Ar^2 is phenyl, wherein Ar^2 is unsubstituted or substituted with C_1-C_4 alkyl, carboxy or halo.

31. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XIII



XIII

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^4 is -(CO)NHOH or -N(OH)COH;

Y^4 is a bond or a divalent linking group having from 1 to 9 carbon atom(s) and from 0 to 5 heteroatom(s) independently selected from oxygen, sulfur and nitrogen;

Z^2 is $-CR^{41}R^{42}$-, $-NR^{41}$-, -O- or -S-;

A^{10}, A^{11}, A^{12}, A^{13} and A^{14} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, $-COOR^{43}$, $-COR^{43}$, $-NR^{43}R^{44}$, $-SR^{43}$, $-SOR^{43}$, $-SO_2R^{43}$, $-SO_2(OR^{43})$, $-(CO)NR^{43}R^{43}$, $-(CO)NR^{43}(CH_2)_nCOOH$, $-NR^{43}(CO)R^{44}$ or $-(CH_2)_nCOOH$, or any adjacent two of A^{10}, A^{11}, A^{12} and A^{13} form with the benzene ring a fused ring that is saturated or unsaturated, aromatic or non-aromatic, and carbocyclic or heterocyclic, said heterocyclic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s);

n is 1-3;

R^{41}, R^{42}, R^{43} and R^{44} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and

said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy, and fused ring are independently unsubstituted or substituted with one or more substituent(s).

32. The method of claim 31, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, -O-, -S- or $-SO_2-$;

p and q are independently 0-4; provided that when q is 0 and W^2 is $-NR^{49}-$, -O-, -S- or $-SO_2-$, then Z^2 is $-CR^{41}R^{42}-$;

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s); and

A^{10}, A^{11} and A^{12} are each hydrogen.

33. The method of claim 32, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$;

p is 0-4;

q is 0;

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are each hydrogen;

A^{10}, A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen, $-COOR^{43}$, C_1-C_4 alkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl; and

A^{14} is $-COOR^{43}$.

34. The method of claim 32, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is -S-;

p and q are independently 1-4;

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are independently hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl or phenyl;

A^{10}, A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, phenyl, benzyl, phenoxy, benzyloxy or halo, wherein said alkyl, alkenyl, alkynyl, phenyl, benzyl, phenoxy and benzyloxy are independently unsubstituted or substituted with carobxy; and

A^{14} is -COOH.

35. The method of claim 32, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, -O-, -S- or $-SO_2-$;

p and q are independently 0-4, provided that when q is 0 and W^2 is $-NR^{49}-$, -O-, -S- or $-SO_2-$, then Z^2 is $-CR^{41}R^{42}-$;

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s);

A^{10}, A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen; and

A^{14} is benzyl or carboxybenzyl.

36. The method of claim 31, wherein the compound of formula XIII is selected from:

3-*tert*-butyl-5-(2-carboxy-3-hydroxycarbamoyl-propyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-4-hydroxycarbamoyl-butyl)-benzoic acid;

3-(2-carboxy-4-hydroxycarbamoyl-butyl)-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoyl-pentyl)-benzoic acid;

3-(2-carboxy-3-hydroxycarbamoyl-propyl)-benzoic acid;

3-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid methyl ester;

3-(2-carboxy-3-hydroxyamino-propyl)-benzoic acid;

3-(2-carboxy-2-hydroxycarbamoyl-ethyl)-benzoic acid methyl ester;

3-(2-carboxy-5-hydroxycarbamoylmethylsulfanyl-pentyl)-benzoic acid;

3-[2-carboxy-5-(2-hydroxycarbamoyl-ethylsulfanyl)-pentyl]-benzoic acid;

3-[2-carboxy-5-(1-hydroxycarbamoyl-propylsulfanyl)-pentyl]-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoylmethylsulfanyl-pentyl)-benzoic acid;

3-*tert*-butyl-5-(2-carboxy-4-hydroxycarbamoylmethyl-sulfanylbutyl)-benzoic acid;

3-[2-carboxy-5-(hydroxycarbamoylphenylmethyl-sulfanyl)pentyl]-benzoic acid;

3-[2-carboxy-5-(1-hydroxycarbamoylbutylsulfanyl)-pentyl]-benzoic acid;

5-(2-carboxy-5-hydroxycarbamoylmethylsulfanyl-pentyl)-biphenyl-3-carboxylic acid;

3-bromo-5-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-benzoic acid;

3-benzyloxy-5-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-benzoic acid;

3-[2-carboxy-5-(1-hydroxycarbamoyl-2-methyl-propylsulfanyl)-pentyl]-benzoic acid;

3-(2-carboxy-3-hydroxycarbamoylmethyl-sulfanylpropyl)-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-5-phenoxy-benzoic acid;

3-(2-carboxy-6-hydroxycarbamoylmethyl-sulfanylhexyl)-benzoic acid;

3-(2-carboxy-4-hydroxycarbamoylmethyl-sulfanylbutyl)-benzoic acid;

3-[2-carboxy-3-(3-hydroxycarbamoyl-propylsulfanyl)-propyl]-benzoic acid;

3-[2-carboxy-5-(4-hydroxycarbamoyl-butylsulfanyl)-pentyl]-benzoic acid;

3-{2-carboxy-5-[(hydroxy-methyl-carbamoyl)-methylsulfanyl]-pentyl}-benzoic acid;

3-*tert*-butyl-5-[2-carboxy-4-(1-hydroxycarbamoyl-propylsulfanyl)-butyl]-benzoic acid;

3-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-4-chloro-benzoic acid;

3-[2-carboxy-4-(1-hydroxycarbamoyl-propylsulfanyl)-butyl]-benzoic acid;

3-[2-carboxy-3-(1-hydroxycarbamoyl-propylsulfanyl)-propyl]-benzoic acid;

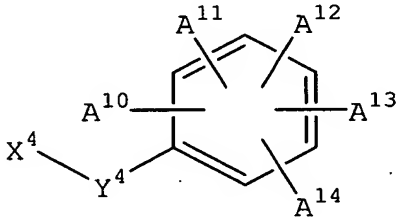
2-biphenyl-3-ylmethyl-5-hydroxycarbamoylmethyl-sulfanyl-pentanoic acid;

3'-(2-carboxy-5-hydroxycarbamoylmethylsulfanyl-pentyl)-biphenyl-3-carboxylic acid;

2-bromo-4-(2-carboxy-5-hydroxycarbamoylmethyl-sulfanylpentyl)-benzoic acid; and

enantiomers and pharmaceutically acceptable equivalents.

37. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XIV



XIV

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^4 is -(CO)NHOH or -N(OH)COH;

Y^4 is a bond or a divalent linking group having from 1 to 9 carbon atom(s) and from 0 to 5 heteroatom(s) independently selected from oxygen, sulfur and nitrogen;

A^{10}, A^{11}, A^{12}, A^{13} and A^{14} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, phenoxy, benzyloxy, hydroxy, halo, nitro, cyano, isocyano, -$COOR^{43}$, -COR^{43}, -$NR^{43}R^{44}$, -SR^{43}, -SOR^{43}, -SO_2R^{43}, -$SO_2(OR^{43})$, -$(CO)NR^{43}R^{44}$, -$(CO)NR^{43}(CH_2)_nCOOH$, -$NR^{43}(CO)R^{44}$ or -$(CH_2)_nCOOH$, or any adjacent two of A^{10}, A^{11}, A^{12} and A^{13} form with the benzene ring a fused ring that is saturated or unsaturated, aromatic or non-aromatic, and carbocyclic or heterocyclic, said heterocyclic ring containing 1 or 2 oxygen, nitrogen and/or sulfur heteroatom(s);

n is 1-3;

R^{43} and R^{44} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle or heterocycle; and

said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy, benzyloxy, and fused ring are independently unsubstituted or substituted with one or more substituent(s).

38. The method of claim 37, wherein:

Y^4 is a bond or $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, -O-, -S- or $-SO_2-$;

p and q are independently 0-4;

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s); and

A^{10}, A^{11} and A^{12} are each hydrogen.

39. The method of claim 37, wherein:

Y^4 is a bond;

A^{10}, A^{11} and A^{12} are each hydrogen;

A^{13} is hydroxy, phenoxy, benzyloxy, $-COOR^{43}$ or $-(CO)NHR^{44}$;

A^{14} is $-COOR^{43}$;

R^{43} is hydrogen, C_1-C_4 alkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl;

R^{44} is benzyl; and

said benzyl, phenoxy and benzyloxy are independently unsubstituted or substituted with $-COOR^{43}$.

40. The method of claim 37, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is -O- or -S-; R^{45}, R^{46}, R^{47} and R^{48} are each hydrogen;

A^{10}, A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen, -COOH, phenyl or benzyloxy, wherein said phenyl and benzyloxy are independently unsubstituted or substituted with $-COOR^{43}$; and

A^{14} is $-COOR^{43}$.

41. The method of claim 37, wherein:

Y^4 is a bond or $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, -O-, -S- or $-SO_2-$;

p and q are independently 0-4;

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s);

A^{10}, A^{11} and A^{12} are each hydrogen;

A^{13} is hydrogen, nitro or C_1-C_4 alkoxy; and

A^{14} is hydroxy, phenoxy, benzyloxy, benzoyl or C_1-C_4 alkoxy, wherein said phenoxy, benzyloxy, benzoyl and alkoxy are independently unsubstituted or substituted with one or more substituent(s).

42. The method of claim 37, wherein the compound is selected from:

5-hydroxycarbamoyl-isophthalic acid monoethyl ester;

6-benzyloxy-N-hydroxy-isophthalamic acid methyl ester;

6,N-dihydroxy-isophthalamic acid;

6-benzyloxy-N-hydroxy-isophthalamic acid;

4-(3-hydroxycarbamoyl-propylsulfanylmethyl)-biphenyl-2,3'-dicarboxylic acid;

4-(4-hydroxycarbamoyl-butylsulfanylmethyl)-biphenyl-2,3'-dicarboxylic acid;

4-(2-hydroxycarbamoyl-ethylsulfanylmethyl)-biphenyl-2,3'-dicarboxylic acid;

3-(2-hydroxycarbamoyl-methylsulfanylethyl)-biphenyl-2,3'-dicarboxylic acid;

5-hydroxycarbamoylmethoxy-isophthalic acid;

3-hydroxycarbamoylmethoxy-benzoic acid;

3-(4-hydroxycarbamoyl-butoxy)-biphenyl-2,3'-dicarboxylic acid;

3-(4-hydroxycarbamoyl-butoxy)-biphenyl-2,3'-dicarboxylic acid;

3-(3-hydroxycarbamoyl-propoxy)-biphenyl-2,3'-dicarboxylic acid;

3-(2-hydroxycarbamoyl-ethoxy)-biphenyl-2,3'-dicarboxylic acid;

3-hydroxycarbamoylmethoxy-biphenyl-2,3'-dicarboxylic acid;

3-hydroxycarbamoylmethoxy-biphenyl-2,3'-dicarboxylic acid dimethyl ester;

2-hydroxycarbamoylmethoxy-benzoic acid;

2-hydroxycarbamoylmethoxy-benzoic acid methyl ester;

3-(2-hydroxycarbamoyl-ethoxy)-biphenyl-2,3'-dicarboxylicacid dimethyl ester;

4-(4-cyano-benzyloxy)-N-hydroxy-benzamide;

3-[3-(2-hydroxycarbamoyl-ethyl)-phenoxymethyl]-benzoic acid;

2,N-dihydroxy-benzamide;

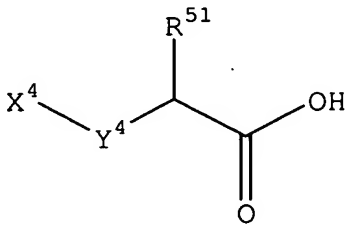
4-(4-fluoro-phenoxy)-N-hydroxy-3-nitro-benzamide;

N-hydroxy-2,5-bis-(2,2,2-trifluoro-ethoxy)-benzamide;

N-hydroxy-2-(4-methyl-benzoyl)-benzamide; and

enantiomers and pharmaceutically acceptable equivalents.

43. The method of claim 1, wherein the NAALADase inhibitor is a compound of formula XV



XV

or an enantiomer or a pharmaceutically acceptable equivalent of said compound, wherein:

X^4 is -(CO)NHOH or -N(OH)COH;

Y^4 is a bond or a divalent linking group having from 1 to 9 carbon atom(s) and from 0 to 5 heteroatom(s) independently selected from oxygen, sulfur and nitrogen; and

R^{51} is hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, C_1-C_9 alkoxy or C_2-C_9 alkenoxy, wherein said alkyl, alkenyl, alkynyl, alkoxy and alkenoxy are independently unsubstituted or substituted with one or more substituent(s); provided that when Y is methylene, amine or oxygen, then R^{51} is not carboxyethyl.

44. The method of claim 43, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$, $-NR^{49}-$, -O-, -S- or $-SO_2-$;

p and q are independently 0-4; and

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are independently hydrogen, C_1-C_9 alkyl, C_2-C_9 alkenyl, C_2-C_9 alkynyl, aryl, heteroaryl, carbocycle, heterocycle, halo, hydroxy, sulfhydryl, nitro, amino, cyano, isocyano, thiocyano, isothiocyano, formamido, thioformamido, sulfo, sulfino, C_1-C_9 alkoxy, C_2-C_9 alkenoxy, phenoxy or benzyloxy, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, heterocycle, alkoxy, alkenyloxy, phenoxy and benzyloxy are independently unsubstituted or substituted with one or more substituent(s).

45. The method of claim 43, wherein:

Y^4 is $-(CR^{45}R^{46})_p-W^2-(CR^{47}R^{48})_q-$;

W^2 is $-CR^{49}R^{50}-$ or -S-;

p is 0-1; q is 0-3; and

R^{45}, R^{46}, R^{47}, R^{48}, R^{49} and R^{50} are each hydrogen.

46. The method of claim 43, wherein the compound of formula XV is 2-(3-hydroxycarbamoyl-methylsulfanyl-propyl)-pentanedioic acid or an enantiomer or a pharmaceutically acceptable equivalent.

47. A pharmaceutical composition comprising:

(i) an effective amount of a NAALADase inhibitor for treating opioid tolerance; and

(ii) a pharmaceutically acceptable carrier.